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## **EUROPEAN PATENT APPLICATION**

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- (a) Date of filing: 16.10.91

① Int CL<sup>5</sup> A61K 31/66, A61K 37/64. A61K 31/675, A61K 31/22, A61K 31/215, A61K 31/19, A61K 31/10, A61K 31/785, A61K 31/455, A61K 31/195, A61K 31/365

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- Date of deferred publication of the search report: 20.10.93 Bulletin 93/42
- (1) Applicant E.R. SQUIBB & SONS, INC. P.O.Box 4000
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- Representative: Josif, Albert, Dr-Ing. et al Baaderstrasse 3 D-80469 München (DE)
- Method for preventing diabetic complications employing a cholesterol lowering drug alone or in combination with an ace inhibitor.
- A method is provided for preventing diabetes and preventing complications resulting from diabetes by administering to a diabetic patient a cholesterol lowering drug, such as pravastatin, alone or in combination with an ACE inhibitor, such as captopril, zofenopril, ceronapril, fosinopril, enalapril or lisinopril.



## PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

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	DOCUMENTS CONSI	DERED TO BE RELEVAN	T	
Category	Citation of document with it of relevant pa	ndication, where appropriate,	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Inc. Cl. 5)
X Y	EP-A-0 272 778 (GL June 1988 * page 3 *  DE-A-2 716 374 (IN		1 2-4,6-8 ,11-31 1	A 61 K 31/66 A 61 K 37/64 A 61 K 31/675 A 61 K 31/22 A 61 K 31/215
Υ	Y APLICADA S.A.) 3 * page 8; page 11 *	November 1977	2-4,6-8 ,11-31	A 61 K 31/19 A 61 K 31/10 A 61 K 31/785 A 61 K 31/455
P,X Y	EP-A-0 414 023 (FU 27 February 1991 * page 3 *	JISAWA PHARM. CO.)	1,2 3,4,6-8 ,11-31	A 61 K 31/195 A 61 K 31/365
The Sear the provision a mee Claims so Claims so Claims to Reason fo	omplete Search  ch Division considers that the present stons of the European Patent Convent aningful search into the state of the a earched completely: carched incompletely: of searched: or the limitation of the search:  e sheet -C-	European patent application does not compion to such an extent that it is not possible to an the hasis of sume of the claims	ly with to carry	TECHNICAL FIELDS SEARCHED (Int. CL5)  A 61 K
X : pai	Plea of search E HAGUE CATEGORY OF CITED DOCUME	E : earlier patent e after the filing	iple underlying the locument, but publi date	lished an, er
A: tec O: no	ricularly relevant if combined with an cument of the same category hnological background n-written disclosure ermediate document	L : document cited	for other reasons	



	CLAIMS INCURRING FEES	
The pre	esent European patent application comprised at the time of filing more than ten claims	
_	All claims thes have been paid within the prescribed time limit. The present European search raport has been	
_	cdrawn up for all claims.	
	Only part of the claims less have been paid within the prescribed time first. The present European search	
	report has been drawn up for the first ten claims and for those claims for which claims fees have been paid.	
	namely claims:	
	No claims fees have been paid within the prescribed time filmit. The present European search report has been	
	drawn up for the first ten claims.	
	ACK OF UNITY OF INVENTION	_
	rch Division considers that the present European patent application does not comply with the requirement of unity of	_
Inventor	and relates to several inventions or groups of inventions,	
namely:		
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	All further search leas have been paid within the fixed time limit. The present European search report has been drawn up for all claims.	
	Only part of the further search fees have been paid within the fixed time limit. The present European search	
	report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid,	
	namely claims:	
X	None of the further search fees has been paid within the fixed time limit. The present European search report	
	has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims,	
	numercums mentioned in item 1	



# PARTIAL EUROPEAN SEARCH REPORT

Application Number

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	DOCUMENTS CONSIDERED TO BE RELEVAN	T	APPLICATION (Int. CI.5)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
х	JPN. J. MED. vol. 29, no. 2, March 1990, pages 156 - 163 T. SASAKI ET AL. 'AMELIORATION OF PROTEINURIA WITH PRAVASTATIN IN HYPERCHOLESTEROLEMIC PATIENTS WITH DIABETES MELLITUS'	1-3,11	
Y	* abstract; page 156; page 160 - page 162 *	4,6-8, 12-31	
X	THE AMERICAN JOURNAL OF CARDIOLOGY vol. 66, no. 8, 18 September 1990, pages 16B - 21B R. GOLDBERG ET AL. 'COMPARISON OF THE EFFECTS OF LOVASTATIN AND GEMFIBROZIL ON LIPIDS AND GLUCOSE CONTROL IN NON-INSULIN-DEPENDENT DIABETES MELLITUS'	1-3-	TECHNICAL FIELDS SEARCHED (Int. CL.5)
Υ	* page 16B; page 20B - page 21B *	4,6-8, 11-31	
X	ATHEROSCLEROSIS vol. 75, no. 1, 1989, pages 67 - 72 G. YOSHINO ET AL. 'LONG-TERM TREATMENT OF HYPERCHOLESTEROLEMIC NON-INSULIN DEPENDENT DIABETICS (NIDDM) WITH PRAVASTATIN (CS-514)'	1-3	
Y	* the whole document *	6-8,11- 31	
Y	DATABASE WPIL Week 8620, Derwent Publications Ltd., London, GB; AN 86-127658 & JP-A-61 064 701 (MEITO SANGYO KK) 3 April 1986 * abstract *	1,2-4,6 -8,11- 31	
Y	G. THEWS ET AL. 'ANATOMIE PHYSIOLOGIE PATHOPHYSIOLOGIE DES MENSCHEN' 1982 , WISSENSCHAFTL. VERLAGSGESELLSCHAFT MBH , STUTTGART  * page 655 - page 657 * -/-	1,2-4,6 -8,11- 31	



# PARTIAL EUROPEAN SEARCH REPORT Application Number

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	DOCUMENTS CONSIDERED TO BE RELEVA	ANT	CLASSIFICATION OF TH APPLICATION (Int. Cl.5)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claum	
Y	WIENER MEDIZINISCHE WOCHENSCHRIFT vol. 139, no. S105, 1989, pages 9 - 17 G. BIESENBACH 'FETTSTOFFWECHSELSTWRUNGEN BEI DIABETES MELLITUS' * the whole document *	1,2-4,6 -8,11- 31	
Y	EP-A-O 000 124 (THERA) 10 January 1979 * claims 1-4 *	12-31	
Y	EP-A-0 331 014 (THERA) 6 September 1989 * column 1; claim 1 *	12-31	
Y	EP-A-0 363 671 (F. HOFFMANN-LA ROCHE AG) 18 April 1990	12-31	TECHNICAL FIELDS SEARCHED (Int. Cl.5)
:			

EPO PORM 1503 03 82 (P0410)



## LACK OF UNITY OF INVENTION

European Patent

Office

The Search Division considers that the present European patent application does not comply with the requirement of unity of invention and relates to several inventions or groups of inventions, namely:

The problem the application tries to solve is to prevent diabetes or to prevent or reduce the risk of complications resulting from diabetes.

The proposed solution is to use cholesterol lowering drugs.

Documents nos. 1 and 2 cited in the Search Report describe the use of cholesterol lowering drugs for the wanted effect.

Therefor the general idea of using cholesterol lowering drug for preventing diabetes or diabetic complications is not new and in view of the state of the art the problem has to be redefined as finding further lipid lowering drugs for preventing diabetes or preventing or reducing the risk of complications resulting from diabetes.

The proposed compounds are structurally and concerning their mode of action not so related as to form a single inventive concept.

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1. Claims 1,12-15,17,19,21,23,26,29 (partially)

2-4,6-8,11,16,18,20,22,24,25,27,28,30,31 (completely)

Use of a HMG CoA reductase inhibitor alone or in combination with an ACE inhibitor for manufacturing a medicament for preventing diabetes or preventing or reducing the risk of complications resulting from diabetes

2. Claims 1,12-15,17,19,21,23,26,29 (partially)

5 (completely)

Use of a squalene synthetase inhibitor alone or in combination with an ACE inhibitor for manufacturing a medicament for preventing diabetes or preventing or reducing the risk of complications resulting from diabetes



#### LACK OF UNITY OF INVENTION

European Patent Office

The Search Division considers that the present European patient application dose not comply with the requirement of unity of invention and relates to several inventions or groups of inventions.

Use of a fibric acid derivative (gemfibrozil, fenofibrate, clofibrate, bezafibrate, ciprofibrate, clinofibrate) alone or in combination with an ACE inhibitor for manufacturing a medicament for preventing diabetes or preventing or reducing the risk of complications resulting from diabetes

- 4. Claims 1,10,12-15,17,19,21,23,26,29 (partially)
  Use of probucol alone or in combination with an ACE inhibitor for manufacturing a medicament for preventing diabetes or preventing or reducing the risk of complications resulting from diabetes
- 5. Claims 1,10,12-15,17,19,21,23,26,29 (partially)
  Use of dextrothyroxine and its sodium salt alone or in combination with an ACE inhibitor for manufacturing a medicament for preventing diabetes or preventing or reducing the risk of complications resulting from diabetes
- 6. Claims 1,10,12-15,17,19,21,23,26,29 (partially)
  Use of Bile acid sequestrants (cholestyramine, colestipol) alone or in combination with an ACE inhibitor for manufacturing a medicament for preventing diabetes or preventing or reducing the risk of complications resulting from diabetes
- 7. Claims 1,10,12-15,17,19,21,23,26,29 (partially)
  Use of nicotinic acid alone or in combination with an ACE inhibitor for manufacturing a medicament for preventing diabetes or preventing or reducing the risk of complications resulting from diabetes
- 8. Claims 1,10,12-15,17,19,21,23,26,29 (partially)
  Use of neomycin alone or in combination with an ACE inhibitor for manufacturing a medicament for preventing diabetes or preventing or reducing the risk of complications resulting from diabetes
- 9. Claims 1,10,12-15,17,19,21,23,26,29 (partially)
  Use of salicylic acid derivatives (p-amino-salicylic acid, acetylsalicylic acid) alone or in combination with an ACE inhibitor for manufacturing a



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#### LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirement of unity of inventions and relates to several inventions or groups of inventions, namely:

medicament for preventing diabetes or preventing or reducing the risk of complications resulting from diabetes



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A compound cannot be defined by its activity (e.g. cholesterol lowering, HMG CoA reductase inhibiting, ACE-inhibiting etc.)

This characterization as well as descriptions of substances as analogs or derivatives of other compounds and the use of huge Markush formulas does not make clear which substances are meant.

The search therefor had to be restricted to the compounds which are explicitly mentioned in the claims and the general inventive idea.

Please note that this restriction is also valid for possible further search for the subjects not searched now because of non-unity. (see sheet B). (Art. 84 EPC)

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